CHEMISTRY LETTERS, pp. 1733-1736, 1983.

A NEW METHOD FOR THE STEREOSELECTIVE SYNTHESIS OF β-XYLOFURANOSIDE

Masahiro MURAKAMI and Teruaki MUKAIYAMA*

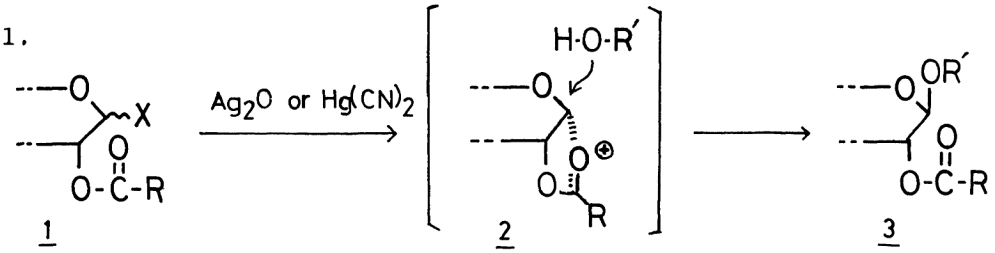
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

β-Xylofuranosides are stereoselectively synthesized in good yields by the successive treatment of the thiocarbonate, derived from 3,5-di-O-benzyl-D-xylofuranose, with methyl fluorosulfonate and hydroxy compounds in the presence of cesium fluoride.

Stereoselective synthesis of O-glycosidic bonds is one of the most important problems in the synthesis of carbohydrates and several efficient methods[1] have been developed.

For the synthesis of 2-O-acylated 1,2-trans-glycoside, the Koenigs-Knorr[1d] reaction is generally employed. It involves the generation of active acyloxonium ion (2) by treating 2-O-acylated glycosyl halides with heavy metal salts such as Ag_2O and $Hg(CN)_2$. The stereoselectivity is principally achieved by the neighboring group participation of 2-acyloxy substituent (Scheme 1).

Scheme 1.



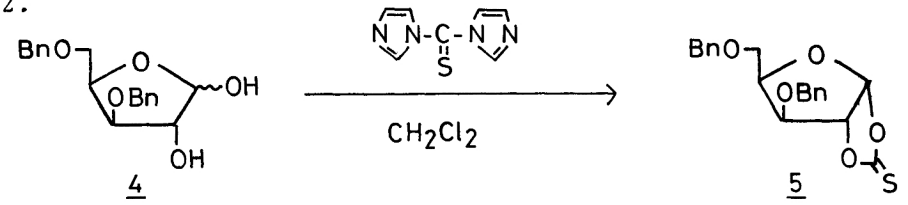
1 2 3

The generation of the similar activated intermediates could be expected by alkylation of thiocarbonates derived from 1,2-unprotected sugars without using heavy metal salts. Based on this assumption, we investigated the new method for the preparation of β-xylofuranoside through the thiocarbonate (5) easily derived from 3,5-di-O-benzyl-D-xylofuranose (4).

In the first place, the thiocarbonate (5) was prepared by the following procedure (Scheme 2): To a dry dichloromethane solution (30 ml) of 3,5-di-O-benzyl-D-xylofuranose (4, 2.35 g, 7.1 mmol)[2] was added 1,1'-thiocarbonyldiimidazole (1.52 g, 8.8 mmol) as powder at 0 °C under an argon atmosphere. After stirring for 2 h at room temperature, the resulting solution was treated with dilute aqueous HCl solution and the organic materials were extracted with dichloromethane. The solvent was evaporated and the residue was purified by column chromatography (silica gel) to give 3,5-di-O-benzyl-1,2-O-thiocarbonyl-α-D-xylofuranose (5, pale yellow oil, 2.28 g, 86%). Found: C, 64.59; H, 5.19;

S, 8.40%. Calcd for $C_{20}H_{20}O_5S$: C, 64.50; H, 5.41; S, 8.61%; ^{1}H-NMR ($CDCl_3$) δ 3.69 (2H, d, J = 5 Hz), 4.0-4.6 (6H, m), 4.96 (1H, d, J = 5 Hz), 6.24 (1H, d, J = 5 Hz), 7.18 (10H, s); IR (neat) 1310, 1270 cm^{-1}; $[\alpha]_D^{24}$ = +20.4° (c 0.55, CH_2Cl_2).

Scheme 2.



Bn = $-CH_2Ph$

Next, we screened the reagents for the alkylation of the thiocarbonate (5) such as methyl iodide, allyl p-toluensulfonate, methyl chlorosulfonate, methyl fluorosulfonate etc. in the reaction of 5 with 2-propanol. And it was found that methyl fluorosulfonate gave the desired products (9b and 10b) in about 60% yield, but the stereoselectivity was not high (9b : 10b = 6 : 4). This reaction presumably involves methylation of the sulfur of 5 giving the intermediate salt (6) and subsequent S_N2 displacement by alcohol at the anomeric carbon (Scheme 3). It was supposed that the poor stereoselectivity was due to the epimerization catalyzed by fluorosulfonic acid formed during the glycosylation reaction. Then, we searched for the suitable base to capture fluorosulfonic acid and it was found that, among various acid captors, cesium fluoride gave the β-anomer in 87% yield with high stereoselectivity (9b : 10b = > 99 : 1). As previously reported,[3] cesium fluoride seemed to act as both an acid captor and an activator of a protic nucleophile. Under the similar conditions, several β-D-xylofuranosides were prepared in good yields and with high stereoselectivity as shown in Table 1.

Typical experimental procedure is described for the synthesis of propyl 3,5-di-O-benzyl-β-D-xylofuranoside: To a stirred suspension of cesium fluoride (573 mg, 3.8 mmol) in 1,2-dichloroethane (1 ml) was added each 1,2-dichloroethane solution (2 ml) of the thiocarbonate (5, 97 mg, 0.26 mmol), propanol (51 mg, 0.85 mmol), and methyl fluorosulfonate (134 mg, 1.2 mmol) successively. The reaction mixture was stirred at 50 - 60 °C for 30 min. Then 1 mol dm^{-3} aqueous solution (2 ml) of sodium hydroxide and a sufficient amount of methanol for homogenization of the mixture were added at room temperature in order to hydrolyze the carbonates (7, 8) into 2-unprotected glycosides (9, 10). After vigorously stirring for 2 h, the mixture was concentrated under reduced pressure and most of the solvent was removed. The organic materials were extracted with chloroform and dried over sodium sulfate. Then the solvent was removed under reduced pressure and the residual oil was purified by thin layer chromatography (silica gel) to afford propyl 3,5-di-O-benzyl-β-D-xylofuranoside (9a, oil, 87 mg, 90%) and a small amount of the corresponding α-anomer (10a, oil, 0.8 mg, 1%). 9a: ^{1}H-NMR ($CDCl_3$) δ 0.6 - 1.0 (3H, m), 1.1 - 1.8 (2H, m), 2.4 - 2.9 (1H, br), 3.1 - 4.6 (11H, m), 4.80 (1H, d, J = 2 Hz), 7.1 - 7.3 (10H, m); IR (neat) 3430 cm^{-1}. 10a: ^{1}H-NMR ($CDCl_3$) δ 0.7 - 1.0 (3H, m), 1.2 - 1.9 (2H, m), 2.75 (1H, d, J = 7.0 Hz), 3.3 - 4.8 (11H, m), 5.04 (1H, d, J = 4.5 Hz), 7.24 (10H, s); IR (neat) 3530 cm^{-1}.

Scheme 3.

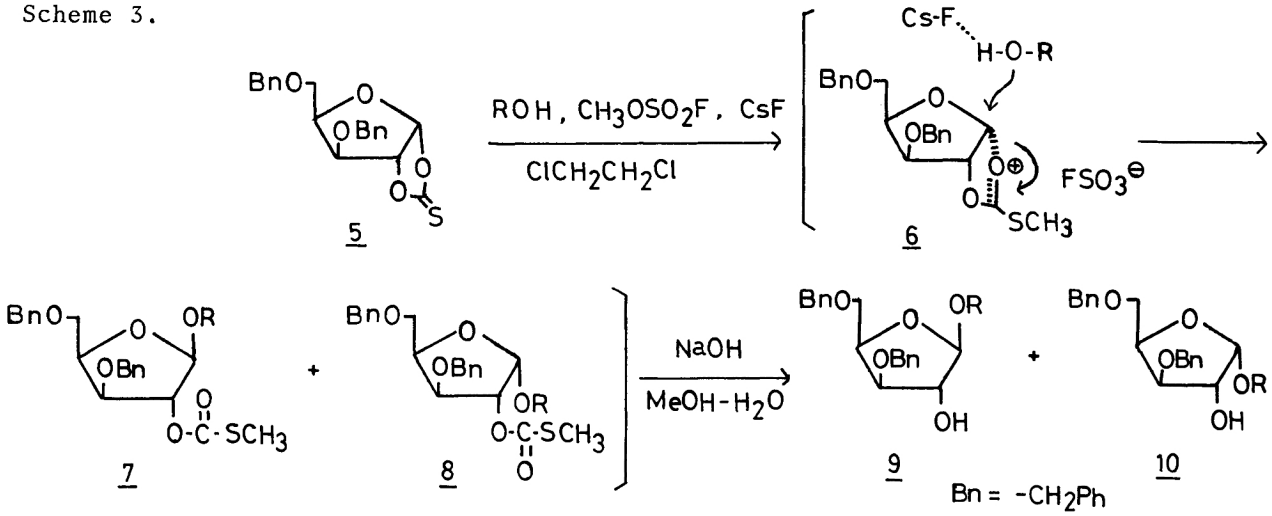
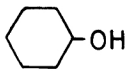
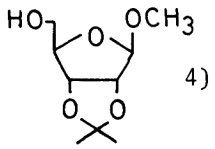


Table 1. Synthesis of Xylofuranosides

Entry	ROH	Yield/%[a]	9 : 10[b]	^{1}H-NMR data[c] 9 δ	9 $J_{1,2}$ / Hz	10[d] δ	10[d] $J_{1,2}$ / Hz
a	n-C_3H_7OH	91	99 : 1	4.80	2.0	5.04	4.5
b	i-C_3H_7OH	87	> 99 : 1	4.88	2.0	5.16	4.5
c	$CH_3OCH_2CH_2OH$	81	> 98 : 2	4.89	1.5	5.08	4.5
d	$PhCH_2CH_2CH_2OH$	75	> 99 : 1	4.79	1.5	4.94	4.5
e		90	98 : 2	4.97	2.0	5.22	4.5
f	 4)	65	e)	——	——	——	——

a) Yields are based on the thiocarbonate (5). All products gave satisfactory ^{1}H-NMR and IR spectra.

b) The anomeric configuration was determined by comparison of the coupling constants ($J_{1,2}$) of anomeric protons. The isomers with $J_{1,2}$ of 1 - 2 Hz and 4 - 5 Hz were assigned to β-anomer (9) and α-anomer (10) respectively; see Ref. 5.

c) Chemical shifts and coupling constants are values of anomeric protons.

d) These data for β-anomers (10) were obtained on the samples prepared by the thiocarbonate method without using cesium fluoride.

e) The isolated product was found to be a single isomer by ^{13}C-NMR spectra,[6] but accurate coupling constant could not be measured because the anomeric proton resonance showed complex pattern.

These results demonstrate that effective activation of anomeric centers of sugars can be achieved by the combination of the corresponding thiocarbonates with methyl fluorosulfonate. The application of this thiocarbonate method to the stereoselective synthesis of various glycosides is under study.

References

1) For examples, see the following: a) G. Wulff and G. Röhle, Angew. Chem., Int. Ed. Engl., 13, 157 (1974);
b) H. Paulsen, ibid., 21, 155 (1982);
c) T. Mukaiyama, Y. Hashimoto, and S. Shoda, Chem. Lett., 1983, 935;
d) W. Koenigs and E. Knorr, Chem. Ber., 34, 957 (1901).
2) 3,5-Di-O-benzyl-D-xylofuranose was prepared by the hydrolysis (H_2O : AcOH : concd HCl = 10 : 15 : 1, 100 °C, 30 min) of 3,5-di-O-benzyl-1,2-O-isopropylidene-α-D-xylose.
3) a) J. H. Clark and J. M. Miller, J. Am. Chem. Soc., 99, 498 (1977);
b) S. Shoda and T. Mukaiyama, Chem. Lett., 1980, 391.
4) Methyl 2,3-O-isopropylidene-β-D-ribofuranoside was prepared by the method of Ishido *et al.*; Chem. Abstr., 63, 7094 e (1965).
5) B. Capon and D. Thacker, Proc. Chem. Soc., 1964, 369.
6) ^{13}C-NMR ($CDCl_3$) δ 25.0 (-O-C($\underline{C}H_3$)$_2$-O-), 26.5 (-O-C($\underline{C}H_3$)$_2$-O-), 54.8 (-O-$\underline{C}H_3$), 68.8, 69.8, 72.1, 73.4, 79.3, 80.0, 82.0, 83.4, 85.0, 85.2, 108.4 (C-1'), 109.3 (C-1), 112.3 (-O-$\underline{C}$(CH$_3$)$_2$-O-), 127.5, 127.6, 127.7, 128.3, 137.9, 138.2.

(Received September 5, 1983)